and, when aa^0 is an arbitrary amino acid residue, said peptide has a disulfide linkage between the second and eleventh cysteine residues; or a salt thereof.--

BASIS FOR THE AMENDMENT

Claims 5 and 7 have been amended.

All of the present amendments are supported by the specification as originally filed. The amendments have been made to insert sequence identifiers, which correspond to the attached sequence listing. No new matter is believed to have been added by these amendments.

REMARKS

Claims 1-40 are pending in the present application.

Applicants have now submitted a Sequence Listing and a corresponding computer readable Sequence Listing. The sequence information recorded in the corresponding computer readable Sequence Listing is identical to the paper copy of the Sequence Listing. Support for all the sequences listed in the Sequence Listing are found in the present application as originally filed. No new matter is believed to have been introduced by the submission of the Sequence Listing and the corresponding computer readable Sequence Listing.

Applicants submit that the present application is ready for examination on the merits. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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Docket No.: **206704US0 PCT**

Serial No: **09/830,559**

IN THE SPECIFICATION

Please amend the specification as follows:

Please replace the formula on page 6, between prenumbered lines 8 and 9, as follows:

--Ac-Cys^{1}-Gly^{2}-AA^{3}-AA^{4}-AA^{5}-AA^{6}-AA^{7}-AA^{8}-Gly^{9}-Cys^{10}-NH_2 [2; SEQ ID NO:1]--

Please replace the formula on page 6, between prenumbered lines 18 and 19, as follows:

--Ac-aa^{0}-Cys^{1}-Gly^{2}-aa^{3}-aa^{4}-aa^{5}-aa^{6}-aa^{7}-Gly^{8}-aa^{9}-Cys^{10}-NH_2 [2b, SEQ ID NO:2]--

Please replace the formula on page 21, between prenumbered lines 1 and 2, as follows:

S———————————————S

--Ac-Cys-Gly-Gln-Leu-Asp-Leu-Ala-Asp-Gly-Cys-NH_2 [2a; SEQ ID NO: 3]--

Please replace the paragraph at page 21, prenumbered lines 4-15, as follows:

--Subsequently, a three-dimensional structure of a complex compound of peptide [2a; SEQ ID NO:3] and a partial structure containing the DNA binding site of AP-1 were prepared by the use of SYBYL, and a molecular dynamics simulation was carried out according to the molecular dynamics calculation program AMBER

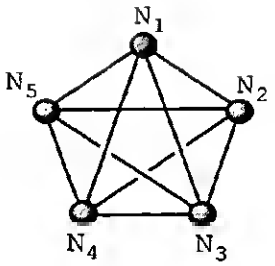
(Oxford Molecular Co., GB) (Fundamentals of Protein Engineering Physics and Chemistry, published by Kyoritsu Shuppan, Page 192, 1991) by using the three-dimensional structure obtained above as an initial structure to obtain a plurality of three-dimensional structures of AP-1-cyclic peptide [2a; SEQ ID NO:3] complex in water.--

Please replace the paragraph at page 21, prenumbered lines 16-23, as follows:

--On the other hand, nuclear magnetic resonance (NMR) spectrum of peptide [2a; SEQ ID NO:3] was measured, and the result was treated according to a structural analysis software X-PLOR (MSI Co., USA) to obtain a plurality of three-dimensional structures of peptide [2a; SEQ ID NO:3] in water experimentally (Shinsei Kagaku Jikken Koza I, Proteins III, Pages 139-147, 1990, published by Tokyo Kagaku Dojin).--

Please replace the paragraph at page 21, prenumbered line 24, to page 22, prenumbered line 21, as follows:

--The experimentally obtained three-dimensional structures were compared with the three-dimensional structures of cyclic peptide [2a; SEQ ID NO:3] in the complex obtained from the molecular dynamics simulation. As a result, a high level of similarity was found out between eleven of the experimentally confirmed three-dimensional structures and fourteen of the three-dimensional structures obtained from molecular dynamics simulation in the partial three-dimensional structure of Gln-Leu-Asp-Leu-Ala [SEQ ID NO: 4]. Based on this finding, it could be confirmed that the five atoms N_1, N_2, N_3, N_4 and N_5 expressed by the following formula:



wherein N_1 represents an atom to which a donative hydrogen atom in a hydrogen-bond donating group is bonded or a hydrogen-bond accepting atom in a hydrogen-bond accepting group; N_3 represents a hydrogen-bond accepting atom in a hydrogen-bond accepting group; and N_2, N_4 and N_5 independently represent an arbitrary carbon atom constituting a hydrophobic group, constitute a pharmacophore necessary for the binding to AP-1 and the expression of an antagonistic activity to AP-1 binding sequence (Souyaku Kagaku, Kagaku Dojin, Pages 11-13, 1995).--

Please replace the list at page 52, prenumbered line 12, to page 53, prenumbered line 28, as follows:

--As typical compounds of this invention, the following compounds can be referred to, for example, provided that Ac represents an acetyl group.

- Ac-Cys-Gly-Gln-Leu-Asp-Leu-Ala-Leu-Gly-Cys-NH_2 [SEQ ID NO:5] (having a disulfide linkage between the first and tenth L-cysteine residues)
- Ac-Cys-Gly-Gln-Leu-Ser-Leu-Ala-Leu-Gly-Cys-NH_2 [SEQ ID NO:6] (having a disulfide linkage between the first and tenth L-cysteine residues)
- Ac-Cys-Gly-Gln-Leu-Asp-Leu-Ala-Gly-Gly-Cys-NH_2 [SEQ ID NO:7] (having a disulfide linkage between the first and tenth L-cysteine residues)
- Ac-Cys-Gly-Gln-Leu-Asp-Leu-Ala-Asn-Gly-Cys-NH_2 [SEQ ID NO:8] (having

a disulfidc linkage between the first and tenth L-cysteine residues)

• Ac-Cys-Gly-Gln-Leu-Ser-Leu-Ala-Asp-Gly-Cys-NH_2 [SEQ ID NO:9] (having a disulfide linkage between the first and tenth cysteine residues)

• Ac-Cys-Gly-Asn-Leu-Asp-Leu-Ala-Asp-Gly-Cys-NH_2 [SEQ ID NO:3] (having a disulfide linkage between the first and tenth L-cysteine residues)

• Ac-Asn-Cys-Gly-Asn-Leu-Leu-Ala-Leu-Gly-Ser-Cys-NH_2 [SEQ ID NO:10] (having a disulfide linkage between the second and eleventh L-cysteine residues)

• Ac-Cys-Gly-Asn-Leu-Leu-Ala-Leu-Gly-Ser-Cys-NH_2 [SEQ ID NO:11] (having a disulfide linkage between the first and tenth L-cysteine residues)

• Ac-Asn-Cys-Gly-Asn-Ala-Leu-Ala-Leu-Gly-Ser-Cys-NH_2 [SEQ ID NO:12] (having a disulfide linkage between the second and eleventh L-cysteine residues)

• Ac-Cys-Gly-Asn-Leu-Leu-Ala-Leu-Gly-Asp-Cys-NH_2 [SEQ ID NO:13] (having a disulfide linkage between the first and tenth L-cysteine residues)

• Ac-Cys-Gly-Asn-Leu-Leu-Ser-Leu-Gly-Asp-Cys-NH_2 [SEQ ID NO:14] (having a disulfide linkage between the first and tenth L-cysteine residues)--

Please replace the paragraph at page 96, prenumbered lines 7-22, as follows:

--The peptide-bonded resin of general formula [7; SEQ ID NO:1] can be obtained by subjecting the resin of general formula [6] to a solid phase method. The construction of peptide chain by solid phase method is carried out by repeating a condensation of amino acid having an amino acid functional group protected with appropriate protecting group and de-protection of the protecting group of α-amino acid. Condensation of amino acid is carried out successively one by one from the terminal amino acid according to the order of amino acids in the sequence to be

synthesized. The procedure of the solid phase method will be mentioned below. A series of reactions used therein are preferably carried out in an atmosphere of nitrogen. Any of the manual method and the method of using an automatic synthesizing apparatus may be adopted.--

Please replace the paragraph at page 99, prenumbered lines 20-25, as follows:

--(4) The peptide of general formula (7; SEQ ID NO:1) can be obtained by acetylating a peptide-bonded resin having 10 residues. Concretely, it can be obtained by reacting a peptide-bonded resin of 10 residues with acetic anhydride in the presence or absence of an amine.--

Please replace the paragraph at page 100, prenumbered lines 16-19, as follows:

--The peptide of general formula [8; SEQ ID NO:1] can be obtained by removing the protecting group of amino side chain and the resin from the protected peptide resin of general formula [7; SEQ ID NO:1] in the presence of an acid.--

Please replace the paragraph at page 101, prenumbered lines 21-26, as follows:

--The cyclic peptide of general formula [2; SEQ ID NO:1] can be obtained by forming a disulfide linkage between the cysteine side chains of the peptide of general formula [8; SEQ ID NO:1]. The formation of intramolecular disulfide linkage between two cysteine residues can be effected according to a known method.--

Please replace the paragraph at page 102, prenumbered lines 12-23, as follows:

--The cyclic peptides of general formula [2; SEQ ID NO:1] or salts thereof thus obtained can be isolated and purified according to conventional methods such as extraction, crystallization, gel filtration, liquid chromatography and/or column chromatography. For example, the isolation and purification can be effcted by the gel filtration method using a gel filter such as Sephadex G-10, G-25 or the like, the column chromatography using a reverse phase type synthetic polymer resin or a chemically modified silica gel carrier and/or a high performance liquid chromatography, or the like.--

Please replace the paragraph at page 102, prenumbered lines 25-27, as follows:

--The cyclic peptide of general formula [2b; SEQ ID NO:2] can be obtained by the same method as Production Process 1.--

Substitute page 384 (Abstract), after the last line, beginning at a new page, please insert the attached sequence listing.

IN THE CLAIMS

Please amend the claims as follows:

--5. (Amended) A peptide of 10 residues represented by the following amino acid sequence:

Ac-Cys^{1}-Gly^{2}-AA^{3}-AA^{4}-AA^{5}-AA^{6}-AA^{7}-AA^{8}-Gly^{9}-Cys^{10}-NH$_2$ [SEQ ID NO:1]

wherein Ac represents an acetyl group, AA^{3} represents a polar amino acid residue, each of AA^{4}, AA^{6} and AA^{7} represents a hydrophobic amino acid residue, AA^{5} represents an amino acid residue having carboxyl or hydroxyl group in the side chain thereof, and AA^{8} represents an arbitrary amino acid residue; said peptide

having a disulfide linkage between the first and tenth cysteine residues; or a salt thereof.--

--7. (Amended) A peptide of 10 or 11 residues represented by the following amino acid sequence:

$Ac\text{-}aa^{0}\text{-}Cys^{1}\text{-}Gly^{2}\text{-}aa^{3}\text{-}aa^{4}\text{-}aa^{5}\text{-}aa^{6}\text{-}aa^{7}\text{-}Gly^{8}\text{-}aa^{9}\text{-}Cys^{10}\text{-}NH_2$ [SEQ ID NO:2]

wherein Ac represents an acetyl group, aa^0 represents an arbitrary amino acid residue or a bonding unit, aa^3 represents a polar amino acid residue, each of aa^4, aa^5 and aa^7 represents a hydrophobic amino acid residue, aa^6 represents an arbitrary amino acid residue, and aa^9 represents an amino acid residue having carboxyl or hydroxyl group in the side chain thereof; provided that, when aa^0 is a bonding unit, said peptide has a disulfide linkage between the first and tenth cysteine residues and, when aa^0 is an arbitrary amino acid residue, said peptide has a disulfide linkage between the second and eleventh cysteine residues; or a salt thereof.--

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